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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,761	01/21/2005	Tomi Jarvinen	HORMOS-019	2621

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EXAMINER	
GOON, SCARLETT Y	

ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,761	JARVINEN ET AL.	
	Examiner	Art Unit	
	SCARLETT GOON	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to Applicants' Amendment and Remarks filed on 11 January 2010 in which claims 1-12 and 21 were cancelled, and claim 14 is amended to change the scope and breadth of the claims.

Claims 13-20 are currently pending and are examined on the merits herein.

Priority

This application is a National Stage entry of PCT/FI03/00511 filed on 24 June 2003 and claims priority to Finland foreign application 20021545 filed on 29 August 2002. A certified copy of the foreign priority document in English has been received.

Rejections Withdrawn

Applicants' amendment, filed 11 January 2010, with respect to the rejection of claim 14 under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention, has been fully considered and is persuasive because the claim has been amended to recite that a cyclodextrin derivative is to be selected from the group as recited in the instant claims. This rejection has been **withdrawn**.

Applicants' amendment, filed 11 January 2010, with respect to the rejection of claims 13-21 under 35 USC § 103(a), as being unpatentable over U.S. Patent 6,451,849 B1 to Ahotupa *et al.*, in view of journal publication by Loftsson *et al.*, in view of U.S. Patent No. 5,336,496 to Akimoto *et al.*, have been fully considered and is

persuasive because the lignans disclosed in the Akimoto '496 patent are structurally different from hydroxymatairesinol in the instantly claimed invention. Thus, one of ordinary skill in the art would have no motivation or suggestion to substitute one of the lignans disclosed in the Akimoto '496 patent with HMR. This rejection has been **withdrawn**.

In view of the cancellation of claims 1-12 and 21, all rejections made with respect to claims 1-12 and 21 in the previous Office Action are withdrawn. This rejection has been **withdrawn**.

The following are new grounds of rejections.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Section [0001]

Claims 13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over PG Pub No. US 2002/0061854 A1 to Ahotupa *et al.* (PTO-892, Ref. A), in view of journal publication by Loftsson *et al.* (of record).

Ahotupa *et al.* teach a pharmaceutical preparation comprising an effective amount of hydroxymatairesinol, a geometric isomer or a stereoisomer thereof, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier (paragraph 0014). Ahotupa *et al.* also teach a food product comprising hydroxymatairesinol, a geometric isomer or a stereoisomer thereof, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier (paragraph 0015 and 0016). The pharmaceutical preparation is preferably an oral formulation. Typical dosage forms include, but are not limited to, oral dosage forms such as powders, granules, capsules, tablets, caplets, lozenges, liquids,

elixirs, emulsions and suspensions. All such dosage forms may include conventional carriers, diluents, excipients, binders and additives known to those skilled in the medicinal and pharmaceutical arts (paragraph 0025). The pharmaceutical carriers typically employed may be solid or liquid. Thus, for example, solid carriers include polysaccharides, while liquid carriers include aqueous solutions of salts, polysaccharides, complexing agents, surfactants, syrups, vegetable oils and certain alcohols (paragraph 0026). However, any pharmaceutically acceptable solid or liquid carrier can be used in the pharmaceutical preparation, except that the formulation cannot be a mixture of only the active agent and plain water (paragraph 0026). When the composition is used as an additive to foods, the carrier can be any non-toxic solid or liquid carrier acceptable for use in food and suitable to be admixed with hydroxymatairesinol (paragraph 0027). Typical solid carriers includes polysaccharides and typical liquid carriers include aqueous solutions of salts, polysaccharides, complexing agents, surfactants, syrups, vegetable oils and certain alcohols (paragraph 0028). However, any acceptable solid or liquid carrier can be used in the food additive, except that the formulation cannot be a mixture of only the active agent and plain water (paragraph 0028). The food product is preferably a functional food, a nutritional supplement, a nutrient, a pharmafood, a nutraceutical, a health food, a designer food or any food product (paragraph 0029). The composition may also be used as a dietary supplement (paragraph 0069).

Although Ahotupa *et al.* teach a pharmaceutical composition comprising hydroxymatairesinol in combination with a pharmaceutically acceptable carrier that

includes polysaccharides, the teachings of Ahotupa *et al.* differ from that of the instantly claimed invention in that Ahotupa *et al.* do not expressly teach cyclodextrins as the polysaccharide carrier.

Loftsson *et al.* teach that cyclodextrins are frequently regarded as a new group of pharmaceutical excipients, although they have been known for over 100 years. Highly purified cyclodextrins and cyclodextrin derivatives are well suited as pharmaceutical excipients (p. 1017, column 1). Cyclodextrins can interact with appropriately sized molecules to result in the formation of inclusion complexes. These noncovalent complexes offer a variety of physiochemical advantages over the unmanipulated drugs including the possibility for increased water solubility and solution stability (p. 1017, abstract). Additionally, the cyclodextrins can be used to increase bioavailability of the drugs, or be used to convert liquid drugs into microcrystalline powders or prevent drug-drug or drug-additive interactions (p. 1017, column 2, first bridging paragraph). The most common cyclodextrins include the natural cyclodextrins, α-, β-, and γ-cyclodextrin (p. 1017, column 2, second paragraph). The natural cyclodextrins can be modified to increase their water solubility, such as by alkylation or hydroxyalkylation of the cyclodextrin hydroxyl groups (p. 1018, column 1). Examples of modified cyclodextrins are shown in Table 2, including alkylated and hydroxyalkylated derivatives (p. 1019, column 1). The most common pharmaceutical application of cyclodextrins is to enhance drug solubility in aqueous solutions (p. 1020, column 2, first paragraph). The solubilizing effects of various cyclodextrins on three different drugs are shown in Table 5 (p. 1021). Cyclodextrins are thus useful as tools to generate aqueous drug solutions

without the use of organic cosolvents, surfactants, or lipids, as formulation adjuncts which increase dissolution rates and oral bioavailability of solid drug complexes, and as materials used to generate safe iv dosage forms intended to provide important pharmacokinetic information or act as potential drug products per se (p. 1024, column 2).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Ahotupa *et al.*, concerning a pharmaceutical preparation comprising an effective amount of hydroxymatairesinol, a geometric isomer or a stereoisomer thereof, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier, with the teachings of Loftsson *et al.*, regarding the use of cyclodextrins as pharmaceutical excipients. Since Ahotupa *et al.* teach that a pharmaceutically acceptable carrier includes polysaccharides known in the art, and Loftsson *et al.* teach that cyclodextrins are useful as pharmaceutical excipients, one of ordinary skill in the art would have been motivated to combine the teachings and select any of the cyclodextrins as the pharmaceutically acceptable carrier in the pharmaceutical preparation disclosed by Ahotupa *et al.*, in order to receive the expected benefit, as suggested by Loftsson *et al.*, that the use of cyclodextrins as a pharmaceutically acceptable excipient offers many advantages, including their ability to increase drug bioavailability, generate aqueous drug solutions without the use of organic cosolvents, surfactants, or lipids, as formulation adjuncts which increase dissolution rates and oral bioavailability of solid drug complexes, and as materials used to generate safe iv dosage forms intended to provide important pharmacokinetic

information or act as potential drug products per se (p. 1024, column 2). Furthermore, as Ahotupa *et al.* teach that any pharmaceutically acceptable solid or liquid carrier can be used in the pharmaceutical preparation, such as polysaccharides, and Loftsson *et al.* teach that cyclodextrins are known pharmaceutically acceptable excipients, one of ordinary skill in the art would have had a reasonable expectation of success in formulating a pharmaceutical composition comprising hydroxymatairesinol and a cyclodextrin, thereby forming an inclusion complex.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Section [0002]

Claims 13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over PG Pub No. US 2001/0016590 A1 to Ahotupa *et al.* (PTO-892, Ref. B), in view of journal publication by Loftsson *et al.* (of record).

Ahotupa *et al.* teach a pharmaceutical preparation comprising an effective amount of hydroxymatairesinol, a geometric isomer or a stereoisomer thereof, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier (paragraph 0013). The pharmaceutical preparation is preferably an oral formulation (paragraph 0023). Ahotupa *et al.* also teach a food product comprising hydroxymatairesinol, a geometric isomer or a stereoisomer thereof, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier (paragraph 0014). The food product is preferably a functional food, a

nutritional supplement, a nutrient, a pharmafood, a nutraceutical, a health food, a designer food or any food product (paragraph 0025). The composition may also be used as a dietary supplement (paragraph 0080).

Although Ahotupa *et al.* teach a pharmaceutical composition comprising hydroxymatairesinol in combination with a pharmaceutically acceptable carrier, the teachings of Ahotupa *et al.* differ from that of the instantly claimed invention in that Ahotupa *et al.* do not expressly teach cyclodextrins as the carrier.

The teachings of Loftsson *et al.* were as disclosed in section [0001] above of the claim rejections under 35 USC § 103.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Ahotupa *et al.*, concerning a pharmaceutical preparation comprising an effective amount of hydroxymatairesinol, a geometric isomer or a stereoisomer thereof, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier, with the teachings of Loftsson *et al.*, regarding the use of cyclodextrins as pharmaceutical excipients. Since Loftsson *et al.* teach that cyclodextrins are useful as pharmaceutical excipients, one of ordinary skill in the art would have been motivated to combine the teachings and select any of the cyclodextrins as the pharmaceutically acceptable carrier in the pharmaceutical preparation disclosed by Ahotupa *et al.*, in order to receive the expected benefit, as suggested by Loftsson *et al.*, that the use of cyclodextrins as a pharmaceutically acceptable excipient offers many advantages, including their ability to increase drug bioavailability, generate aqueous drug solutions without the use of organic cosolvents,

surfactants, or lipids, as formulation adjuncts which increase dissolution rates and oral bioavailability of solid drug complexes, and as materials used to generate safe iv dosage forms intended to provide important pharmacokinetic information or act as potential drug products per se (p. 1024, column 2). Furthermore, as Ahotupa *et al.* teach that any pharmaceutically acceptable solid or liquid carrier can be used in the pharmaceutical preparation and Loftsson *et al.* teach that cyclodextrins are known pharmaceutically acceptable excipients, one of ordinary skill in the art would have had a reasonable expectation of success in formulating a pharmaceutical composition comprising hydroxymatairesinol and a cyclodextrin, thereby forming an inclusion complex.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Response to Arguments

Applicants' amendment, filed 11 January 2010, with respect to the rejection of claims 13-21 under 35 USC § 103(a), as being unpatentable over U.S. Patent 6,451,849 B1 to Ahotupa *et al.*, in view of journal publication by Loftsson *et al.*, in view of U.S. Patent No. 5,336,496 to Akimoto *et al.*, have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made as indicated above.

Specifically, Ahotupa *et al.* teach pharmaceutical compositions and food products comprising hydroxymatairesinol and a pharmaceutically acceptable carrier, such as

polysaccharides and Loftsson *et al.* teach that cyclodextrins are known pharmaceutically acceptable excipients. Thus, one of ordinary skill in the art would have been motivated to use cyclodextrins as the pharmaceutically acceptable carrier in the compositions disclosed by Ahotupa *et al.*, and furthermore, would have a reasonable expectation of success, as discussed in the rejections above.

Conclusion

No claim is allowed. This rejection is made NON-FINAL due to the new/modified grounds of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SCARLETT GOON whose telephone number is 571-270-5241. The examiner can normally be reached on Mon - Thu 7:00 am - 4 pm and every other Fri 7:00 am - 12 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623

/SCARLETT GOON/
Examiner
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